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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/708,352	11/08/2000	Joan D. Leonard	02108.0001U2	1597

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EXAMINER

FORD, VANESSA L

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 05/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	09/708,352		LEONARD ET AL.	
	Examiner		Art Unit	
	Vanessa L. Ford		1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3-12 and 29-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-12 and 29-56 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 08 November 2000 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4/22/04</u> . | 6) <input type="checkbox"/> Other: _____ |

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FINAL ACTION

1. This Office Action is responsive to Applicant's amendment and response filed August 19, 2004. Claims 1, 3-8 and 10-12 have been amended. Claims 2 and 13-28 have been cancelled. Claims 29-56 have been added.

Rejections Withdrawn

2. In view of Applicant's amendment and response the following Objection and Rejections have been withdrawn:

- a) Objection to claim 22, page 3, paragraph 2 of previous Office action.
- b) Objection to claim 21, page 3 paragraph 4 of previous Office action.
- c) Rejection of claims 1-12, 21-22 and 24 under 35 U.S.C. 112, first paragraph, pages 3-5 paragraph 5 of previous Office action.
- d) Rejection of claims 8-12, 21-22 and 24 under 35 U.S.C. 112, second paragraph, page 5 paragraph 6 of previous Office action.
- e) Rejection of claims 1-12, 21-22, 24 and 27 under 35 U.S.C. 112, second paragraph, page 6 paragraph 7 of previous Office action.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejections Maintained

4. The rejection of claims 1, 3, 5-6 and newly submitted claims 29-30, 40-44 and 52-55 under 35 U.S.C. 102(b) is maintained for the reasons set forth on pages 6-7 paragraph 8 of the previous Office Action.

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The rejection is on the grounds that the claims are drawn to a vaccine composition which is protective against *Mycoplasma bovis* clinical disease in a bovine species comprising at least one inactivated or attenuated *Mycoplasma bovis* biotype and a pharmaceutically acceptable excipient and wherein the vaccine does not include saponin.

Boothby teaches a vaccine composition comprising killed *Mycoplasma bovis* and phosphate buffered saline (PBS) used for systemic immunization of calves (page 130). Boothby teaches that the vaccine preparations used contained 5.00 mg/ml of antigen for immunization (page 131) which meets the claim limitation "wherein the amount of each inactivated biotype is at least 10^8 *M. bovis* cells". Boothby teaches that cows vaccinated with *M. bovis* antigen in PBS elicited a moderate indirect hemagglutinations (IHA) response to systematic vaccination, an IgG ELISA response and an ELISA IgA response (page 133). Boothby et al teach that the highest respiratory IgA reactivity was found in the nasal secretions of the group which was vaccinated with *M. bovis* in PBS (page 134). Boothby et al teach that there was no sign of respiratory illness in any calves used in the study (page 136). Therefore, the vaccines were protective against respiratory infection caused by *M. bovis*.

Since the Office does not have the facilities for examining and comparing applicant's vaccine with vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the products of the prior art (i.e., that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges there are functional differences between the Boothby and the claimed invention. Applicant teaches that the vaccine of the claimed invention does not cause unfavorable or adverse reactions. Applicant urges that Boothby teaches vaccines that demonstrate unfavorable reactions. Applicant urges that newly submitted claims are not anticipated by Boothby. Applicant urges that newly added claim 29 recites that the vaccine is protective against *Mycoplasma bovis* mastitis. Applicant urges that the characteristic of being protective against mastitis is not simply an intended use but is a characteristic of the vaccine itself. Applicant urges that publications later than Boothby teach that

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Boothby could not have disclosed a vaccine protective against mastitis.

Applicant refers to Heller et al, 1993, Hanson, September 2001 and Hanson, October 2001. Applicant urges that newly submitted claims 34-39 recite "at least two inactivated or attenuated *Mycoplasma bovis* biotypes" and Boothby does not disclose more than a single biotype. Applicant urges that newly submitted claim 52 comprises an adjuvant that differs from the adjuvants listed in Boothby.

Applicant's arguments filed August 19, 2004 have been fully considered but they are not persuasive. The claims are directed to vaccine compositions comprising at least one inactivated *Mycoplasma bovis* biotype and pharmaceutically acceptable excipient. Boothby teaches vaccine compositions comprising at least ^{one} ~~an~~ formalin inactivated *M. bovis* in PBS (pages 40 and 131). Boothby also teaches that adjuvants such as Freund's incomplete adjuvant were used in the vaccine compositions (pages 131-132). Applicant is arguing limitations that are not in the claims with their assertion that "the vaccine compositions of the prior ^{art} cause adverse reactions and the claimed vaccine composition do not". There is no claim limitation regarding favorable, unfavorable or any kind of reactions as they relate to the claimed vaccine compositions. In response to applicant's argument regarding that "the claimed vaccines are protective against *Mycoplasma bovis* mastitis", the Examiner is viewing this limitation as limitation of intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of

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performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). Applicant's referral to other publications (Heller et al, 1993, Hanson, September 2001 and Hanson, October 2001) to support their position is irrelevant since Boothby teach the claimed vaccine compositions. Applicant has not provided a side-by-side comparison to show that the vaccines of the prior art differ from the claimed vaccine. Therefore, it is the Examiner's position that Boothby anticipates the claimed invention. It should be noted that this rejection does not include claims 34-39 which recite "at least two inactivated or attenuated *M. bovis* biotypes.

5. The rejection of claims 1, 4, 5 and 7 and newly submitted claims 29-30 and 56 under 35 U.S.C. 102(b) is maintained for the reasons set forth on pages 8-9 paragraph 9 of the previous Office Action.

The rejection was on the grounds that Thorns et al teach attenuated bovine strains of *M. bovis*. Thorns et al teach that mice were inoculated with 0.1 of E medium (excipient) containing a known number of colony forming units (CFU) of *M. bovis*. Thorns et al teach that the attenuated strains (passaged more than 91-138 times) contained an inoculum per gland of 6.0-7.0 cells (cells measured (\log_{10})(see Table 1, page 329). This amount meets the claim limitation "wherein the amount of each attenuated biotype is at least 10^5 *M. bovis* cells. Thorns et al teach that the *M. bovis* strains were passaged in liquid medium more than 60 times were markedly less virulent than the same or different strains with fewer passages. Thorns et al teach that the high passaged *M. bovis* strains were less virulent and produced only minor histopathological changes in vaccinated animals (see the Abstract). Thorns et al teach that mice inoculated with high passage *M. bovis* did not produce a systemic response (page 331). Thorns et al

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teach that only one out of five in each of the group inoculated with *M. bovis* passaged 91 times showed signs inflammation (page 329, Table 1). Thorns et al teach that all mice that were inoculated with *M. bovis* passaged over 91 times had normal glands and showed not signs of systematic response (page 329, Table 1). Therefore, the mice vaccinated with *M. bovis* passaged over 91 times appeared to be protected against systematic response. Thorns et al teach that the modified strains of *M. bovis* (high passage strains) should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease (page 332).

Since the Office does not have the facilities for examining and comparing applicant's vaccine with vaccine of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the products of the prior art (i.e., that the vaccine of the prior art does not possess the same material structural and functional characteristics of the claimed vaccine). See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant urges that there is no disclosure in Thorns et al that the attenuated strains were protective against any disease. Applicant urges that Thorns et al do not disclose any data that indicates that the attenuated strains cause any stimulation of the immune system in mice against *M. bovis*. Applicant points out the strains themselves were injected into mice. Applicant urges that there are no showing in Thorns et al that the disclosed attenuated *M. bovis* strains could be used as vaccines.

Applicant's arguments filed August 19, 2004 have been fully considered but they are not persuasive. The claims are directed to vaccine compositions comprising at least one attenuated *Mycoplasma bovis* biotype and pharmaceutically acceptable excipient. Thorns et al teach vaccine compositions comprising at least ^{one} ~~an~~ attenuated *M. bovis* biotype in 0.1 E medium (excipient).

In response to applicant's argument regarding protection against any disease and stimulation of the immune system, these are claim limitations that are viewed

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as imitations of intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). Applicant has not provided a side-by-side comparison to show that the vaccines of the prior art differ from the claimed vaccine. Therefore, it is the Examiner's position that Thorns et al anticipate the claimed invention.

6. The rejection of claims 1, 3-12 and newly submitted 29-56 under 35 U.S.C. 103(a) is maintained for the reasons set forth on pages 9-12, paragraph 10 of the previous Office Action.

The rejection was on the grounds that Boothby teaches a vaccine composition comprising killed *Mycoplasma bovis* and phosphate buffered saline used for systemic immunization of calves (page 130). Boothby also teaches vaccine preparations comprising 0.5 ml killed *Mycoplasma bovis* antigen, 1 ml of Freund's incomplete adjuvant and 0.5ml of various aqueous solutions (page 131). Boothby teaches that the vaccine preparations used contained 5.00 mg/ml of antigen for immunization (page 131) which meets the claim limitations "wherein the amount of each inactivated biotype is at least 10^8 *M. bovis* cells". Boothby teaches that *M. bovis* is not highly immunogenic in the bovine. Boothby teaches that immunopotentiating effect of adjuvants may be used to prolonged deposition of antigen, modification the antigen or the recruitment and/or activation of the circulating lymphoid or reticuloendothelial cells (page 129). Boothby teach that adjuvants have been used in successful vaccine preparations of *M. bovis* and other pathogenic mycoplasmas. Boothby further teaches that adjuvants would be of particular benefit if found for local immunization where

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lymphocytes and phagocytic cells are suppressed or where small amounts of antigen is preferred to avoid undesirable reactions (page 129).

Boothby does not teach the use of at least inactivated *M. bovis* biotypes.

Poumarat et al disclose 37 *Mycoplasma bovis* strains from 13 different genomic groups (i.e. biotypes)(see the Abstract). Poumarat et al disclose that based on the combination of the different electrophoretic profiles obtained with the three enzymes, the 37 strains could be classified in 13 genomic groups (table 2).

Boothby and Poumarat et al do not teach the use of attenuated *M. bovis* biotypes.

Thorns et al teach attenuated bovine strains of *M. bovis*. Thorns et al teach that mice were inoculated with 0.1 of E medium containing a known number of colony forming units (CFU) of *M. bovis*. Thorns et al teach that the attenuated strains (passaged more than 60 times) contained an inoculum per gland of 5.1-7.0 cells (cells measured (\log_{10})) (see Table 1, page 329). This amount meets the claim limitation "wherein the amount of each attenuated biotype is at least 10^5 *M. bovis* cells. Thorns et al teach that the *M. bovis* strains were passaged in liquid medium more than 60 times were markedly less virulent than the same or different strains with fewer passages. Thorns et al teach that the high passaged *M. bovis* strains were less virulent and produced only minor histopathological changes in vaccinated animals (see the Abstract). Thorns et al teach that the modified strains of *M. bovis* (high passage strains) should provide further insight into the pathogenesis of *M. bovis* mastitis which could perhaps lead to a stable vaccine for this disease (page 332).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to add the attenuated *M. bovis* strains of a taught by Thorns et al and the multiple *M. bovis* biotype isolates as taught by Poumarat et al and modify the vaccine composition comprising inactivated *M. bovis* and PBS to include a suitable adjuvant because Poumarat et al teach that there is a marked intraspecies genomic heterogeneity among isolates of *Mycoplasma bovis* collected from different geographic origins and that antigenic variability must be taken into account in developing diagnostic and vaccination strategies (page 319) and Thorns et al has demonstrated that high passaged *M. bovis* strains were less virulent and produced only minor histopathological changes in vaccinated animals and do not cause systematic changes in inoculated animals. Additionally, Boothby teaches that immunopotentiating effect of adjuvants may be used to prolonged deposition of antigen, modification the antigen or the recruitment and/or activation of the circulating lymphoid or reticuloendothelial cells (page 129). It would be expected that a vaccine composition comprising inactivated *M. bovis* strains of multiple biotypes, attenuated *M. bovis* strains of multiple biotypes, PBS and a suitable adjuvant would be effect against infections caused by *M. bovis*.

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Applicant urges that Boothby does not disclose a vaccine that does not cause unfavorable reactions or a vaccine that is protective against mastitis. Applicant urges neither Thorns et al or Poumarat et al provide the subject matter that is missing in Boothby. Applicant urges that Thorns et al do not teach vaccines and certainly do not teach vaccines that do not cause unfavorable reactions or vaccines that are protective against mastitis. Applicant urges that Poumarat et al do not disclose any vaccines since Poumarat et al is limited to a study of the antigenic characteristics of certain strains of *Mycoplasma bovis*. Applicant urges that one of skill in the art would not could not arrive at the present invention by combining Thorns et al, Poumarat et al and Boothby.

Applicant's arguments filed August 19, 2004 have been fully considered but they are not persuasive. In response to applicant's argument that one of skill in the art would not have any suggestion to combine the references to arrive at the claimed invention, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). One of skill in the art would have been motivated to combine the teachings of the prior art because Poumarat et al teach that there is a marked intraspecies genomic heterogeneity among isolates of *Mycoplasma bovis* collected from different geographic origins and that antigenic variability must be

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taken into account in developing diagnostic and vaccination strategies (page 319) and Thorns et al has demonstrated that high passaged *M. bovis* strains were less virulent and produced only minor histopathological changes in vaccinated animals and do not cause systematic changes in inoculated animals. Therefore, one of ordinary skill in the art would reasonably conclude that a vaccine composition comprising inactivated *M. bovis* strains of multiple biotypes, attenuated *M. bovis* strains of multiple biotypes, PBS and a suitable adjuvant would be effect against infections caused by *M. bovis*.

To address Applicant's comments regarding that the prior art references do not teach vaccine compositions that do not cause unfavorable reaction, it is the Examiner's position that Applicant is arguing limitations that are not in the claims. There is no claim limitation regarding favorable, unfavorable or any kind of reactions as they relate to the claimed vaccine compositions. To address Applicant's comments that the prior art references do not teach "vaccine compositions that are protective against mastitis", it is the Examiner's position that the claim limitation " the vaccine compositions are protective against *Mycoplasma bovis* clinical disease" is being viewed as a limitation of intended use. It should be remembered that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*,

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370 F.2d 576, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 312 F.2d 937, 939, 136 USPQ 458, 459 (CCPA 1963). To address the claim limitations of the newly submitted claims, such as “biotypes are genetically different as determined by an analysis of DNA or RNA from biotypes”, “wherein the analysis is PCR fingerprinting, analysis of ribosomal RNA or analysis of DNA polymorphisms” “wherein the PCR fingerprinting uses as primer’s SEQ ID NO:1 and SEQ ID NO:2” and “wherein the *M. bovis* biotype is inactivated and had been inactivated by treatment with formalin, azide, freeze-thawing, sonification, heat, sudden pressure drop, detergent, lysozyme, phenol, proteolytic enzymes, β -propiolactone, Thimerosal or binary ethyleneimine” would be viewed as process limitations. It should be remembered that the products of the prior art reference appear to be the same product claimed by the applicant because they appear to possess the same functional characteristics. The purification or production of a product by a particular process does not impart novelty or unobviousness to a product when the same product is taught by the prior art. This is particularly true when properties of the product are not changed by the process in an unexpected manner. See *In re Thorpe*, 227 USPO 964 (CAFC 1985); *In re Marosi*, 218 USPO 289, 29222-293 (CAFC 1983); *In re Brown*, 173 USPO 685 (CCPA 1972). Even if applicant’s product can be shown to be of higher purity than the product of the prior art reference, applicant’s needs to show some unexpected and unique utility or property, such as unexpected biologically significant increase in specific activity with which the increased purity, greater stability and/or practicality or freedom from some restrictive element or adverse side effects

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inherent in the product preparations of the prior art or some other secondary consideration which the additional degree of purity imparts (to which there is a basis in the specification) to applicant's product in order to overcome the aspect of the product's purity is relied upon. There is nothing on the record to show that the combination of reference does not suggest the claimed invention.

Status of Claims

7. No claims allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.


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9. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


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May 12, 2005


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